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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,587	10/21/2004	Guangzhou Zou	1392/10/21 PCT/US	5250
25297 7590 09/07/2007 JENKINS, WILSON, TAYLOR & HUNT, P. A. SUITE 1200, UNIVERSITY TOWER 3100 TOWER BOULEVARD DURHAM, NC 27707			EXAMINER SKOWRONEK, KARLHEINZ R	
			ART UNIT 1631	PAPER NUMBER
			MAIL DATE 09/07/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/500,587	Applicant(s) ZOU ET AL.	
	Examiner Karlheinz R. Skowronek	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06-07-2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6,8-27,29 and 30 is/are pending in the application.
- 4a) Of the above claim(s) 15-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6,8-14 and 29 is/are rejected.
- 7) ☒ Claim(s) 29 and 30 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 June 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/30/2007; 3/21/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Upon further reconsideration, claims 8-14, the invention of group III, have been rejoined with the invention of group I, claims 1-6.

Claim Status

Claims 1-6, 8-27, and 29-30 are pending.

Claims 7 and 28 are cancelled.

Claims 15-27 stand withdrawn as being directed to a non-elected invention.

Claims 1-14 and 29-30 are being examined.

Specification

Response to Arguments

Applicant's arguments, see p. 9, filed 07 June 2007, with respect to objections to the specification regarding trademark usage have been fully considered and are persuasive. The objections of specification with respect to the use of trademarks have been withdrawn.

The following objection is reiterated from a previous action.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded

hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See for example, p. 32, line 13.

Response to Arguments

Applicant's arguments filed 07 June 2007, with respect to the objection to the specification regarding the use of browser executable code have been fully considered but they are not persuasive. The examiner suggests removing ftp:// from the URL to overcome the objection.

The following objection is newly applied.

The disclosure is objected to because of the following informalities: The term "oligo" on page 7, line 9 of the specification is misspelled as "olgo.

Appropriate correction is required.

Claim Objections

Applicant is advised that should claim 8 be found allowable, claim 14 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is unclear with respect to the term "its" in line 5. The term "its" could refer to the correction coefficient, the each oligo probe, or all the measured signals collectively.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6, 8-14, 29, and 30 are drawn to a process. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (*State Street Bank & Trust Co. v. Signature Financial Group Inc.* CAFC 47 USPQ2d 1596 (1998), *AT&T Corp. v. Excel Communications Inc.* (CAFC 50 USPQ2d 1447 (1999)). The instant claims do not result in a physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

As noted in *State Street Bank & Trust Co. v. Signature Financial Group Inc.* CAFC 47 USPQ2d 1596 (1998) below, the statutory category of the claimed subject

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matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result:

The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to -- process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Section 101 specifies that statutory subject matter must also satisfy the other "conditions and requirements" of Title 35, including novelty, nonobviousness, and adequacy of disclosure and notice. See *In re Warmerdam*, 33 F.3d 1354, 1359, 31 USPQ2d 1754, 1757-58 (Fed. Cir. 1994). For purpose of our analysis, as noted above, claim 1 is directed to a machine programmed with the Hub and Spoke software and admittedly produces a "useful, concrete, and tangible result." *Alappat*, 33 F.3d at 1544, 31 USPQ2d at 1557. This renders it statutory subject matter, even if the useful result is expressed in numbers, such as price, profit, percentage, cost, or loss.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be "tangible," the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

Claims 1-6, 8-14, 29, and 30 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the method is outputted to a display or a memory or another computer on a network, or to a user, or by including a physical transformation.

Claim Rejections - 35 USC § 102

Response to Arguments

Applicant's arguments, see p. 12-14, filed 07 June 2007, with respect to rejection of claims 1-5 as anticipated by Fodor et al. have been fully considered and are persuasive. The rejection of claims 1-5 as anticipated by Fodor et al. has been withdrawn.

Response to Arguments

Applicant's arguments, see p. 14, filed 07 June 2007, with respect to the rejection of claims 1-6 as anticipated by Tseng et al. under 35 USC 2102 (a) have been fully considered and are persuasive. The rejection of claims 1-6 has been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

This rejection is newly applied.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jelinsky et al. (Mol. Cell. Biol., Vol. 20, No. 21, p.8157-8167, November 2000), in view of Wolenguth et al. (US PGPUB 2004/0009479).

The claims are directed to a method of correcting probe hybridization signals by measuring signals from each oligo probe in multiple hybridizations; calculating a correction coefficient for the probes such that the signal average is equal to a constant; and correcting the signal for the probes using the calculated correction coefficient. In some embodiments, an average and standard deviation for the signals observed for each probe are calculated. In some embodiments, an uncertainty coefficient, called

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signal to noise ratio, is calculated based on the ratio of the average to standard deviation.

Jelinsky et al. teach a method of correcting oligoprobe hybridization signals (p. 8157, col. 2, para 2, line 1-22). Jelinsky et al. show that 4 arrays of 6218 probes each were incubated with 10ug RNA, washed and scanned (p. 8157, col. 2, para 2, line 2-6). Jelinsky et al. show that a correction coefficient is calculated for the arrays such that the average of the intensities on the array is equal to a constant, 300 (p. 8157, col. 2, line 16-18). Jelinsky et al. teach that the scaling allows the arrays to be directly compared with each other (p. 8157, col. 2, line 18-19).

Jelinsky et al. do not show the calculation of individual correction coefficients for individual probes where the average signal of the individual probes is made to equal a constant.

Wohlgemuth et al. show a method of measuring DNA hybridization. Wohlgemuth et al. teach individual probes or median background subtracted signals (BGSS) can be scaled to be between 0 and 1 [0212]. Wohlgemuth et al. teach that scaling is desirable because it has the advantage of facilitating the comparison of data between different experiments [0212]. Wohlgemuth et al. teach that DNA is genomic DNA [0091]. Wohlgemuth et al. show that an average and standard deviation for the signals observed for each probe are calculated [0207]. Wohlgemuth et al. show that an uncertainty coefficient, called signal to noise ratio, is calculated based on the ratio of the average to standard deviation [0207]. Wohlgemuth et al. show that probes that do not have a certain predetermined signal to noise ratio are disregarded. In Wohlgemuth et

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al., the signal to noise ratio is calculated as mean divided by the standard deviation. The signal to noise ratio is the inverse of the coefficient of variation, standard deviation divided by the mean. Wohlgemuth et al. teach that if the signal to noise ratio is less than 3 which is equivalent to having a coefficient of variation that is greater than 0.33 the data is flagged but used, reading on a predetermined value that is approximately 1.0 [0728]. As the signal to noise ratio decreases, it approaches 1. When the signal to noise ratio is equal to 1, the ratio indicates that signal cannot be distinguished from the noise, indicative of data of poor quality. Similarly for the inverse of the signal to noise ratio, coefficient of variation (CV), as the CV increases to approach 1, the quality of the data becomes poorer and less reliable. Wohlgemuth et al. teach that if a replicate feature is of poor quality it can be disregarded and the remaining features used to represent the gene [0200].

It would have been obvious to one of skill in the art to modify the method of correcting oligo probe hybridization signals of Jelinsky et al. with the individual probe scale factors of Wohlgemuth et al. because Wohlgemuth et al. shows that scaling provides the advantage of facilitating the comparison of data between different experiments. As the signal to noise ratio decreases, it approaches 1. When the signal to noise ratio is equal to 1, the ratio indicates that signal cannot be distinguished from the noise, indicative of data of poor quality. Similarly for the inverse of the signal to noise ratio, coefficient of variation (CV), as the CV increases to approach 1, the quality of the data becomes poorer and less reliable.

This rejection is newly applied.

Claim 8-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jelinsky et al. (Mol. Cell. Biol., Vol. 20, No. 21, p.8157-8167, November 2000), in view of Wolenguth et al. (US PG PUB 2007/0037144) as applied to claims 1-5 above, and further in view of Pinkel et al. (US Pat 5,830,645).

The claims are drawn to determining a dynamic range for DNA binding.

Jelinsky et al. (Mol. Cell. Biol., Vol. 20, No. 21, p.8157-8167, November 2000), in view of Wolenguth et al. (US PG PUB 2007/0037144) as applied to claims 1-5 above do not teach determining a dynamic range for DNA binding.

Pinkel et al. show a method comparative genomic hybridization. Pinkel et al. show that the method provides increased sensitivity, more precise localization of chromosomal abnormalities and which can detect differences in levels of gene expression are particularly desirable for the diagnosis of disease (col. 2, line 23-26). Pinkel et al. show that serial dilutions of pairs of fluorochrome in known relative proportions can also be analyzed to determine the accuracy with which fluorescence ratio measurements reflect actual fluorochrome ratios over the dynamic range permitted by the detectors and membrane fluorescence (col. 8, line 44-49).

It would have been obvious to one of skill in the art to modify the method of correcting oligo probe hybridization signals of Jelinsky et al., in view of Wolenguth et al. as applied to claims 1-5 above and in further view of the method comparative genomic hybridization by Pinkel et al. because Pinkel et al. show that Pinkel et al. show that the method provides increased sensitivity, more precise localization of chromosomal

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abnormalities and which can detect differences in levels of gene expression are particularly desirable for the diagnosis of disease.

Claim 30 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

29 August 2007

/KRS/

Karlheinz R. Skowronek
Assistant Examiner, Art Unit 1631

John S. Brusca 30 August 2007

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER